REMARKS

Applicants have received and reviewed the Office Action dated November 13, 2008. Applicants have amended claims 1, 7, 9, 26 and 30. Support for the amendments can be found in the specification, for example, at the original claims and Example 1 on pages 13-18. Applicants submit no new matter has been added. Applicants have canceled claims 2-5, and 8. Claims 1, 6-7, 9-11, 21, and 26-30 are pending.

35 U.S.C. § 102(b)

Claims 1-3 and 7-8 were rejected under 35 U.S.C. § 102(b) as anticipated by Villa et al., WO 00/76481. Applicants respectfully traverse this rejection. Applicant claims an oral pharmaceutical formulation in the form of a granulate, a coating, and a sachet. *Villa* does not disclose the administration of a granulate with a coating in a sachet. *Villa* discloses the administration of a tablet that is remarkably different from the granulate of the present invention. The granulate of the presently claimed invention is administered as a granulate, not a tablet. The release profile of presently claimed invention is achieved by adjusting the coating to the specific surface area of the granulate to achieve the *in vitro* release characteristics, not by a hydrophilic matrix and the consequent swelling due to the distension of the polymeric chains of the hydrogels in the composition of the *Villa* tablet (*Villa*, Page 6, lines 20-34). The release characteristic of a compressed table must be different than the granulate form claimed.

Without acquiescing to the rejections and solely to expedite the prosecution, Applicants have amended claims 1 and 7 and have canceled claim 2, 3, and 8.

Villa discloses a controlled release oral pharmaceutical compositions containing as active ingredient 5-amino-salicyclic acid (mesalazine) comprising an inner lipophilic matrix consisting of substances with a melting point below 90°C, an outer hydrophilic matrix, and optionally other excipients (Abstract and claim 1).

Villa recites the formation of granules as the first step in the multistep process leading to a tablet formation. Importantly, the granules of *Villa* neither comprise the same ingredients nor

achieve the same release profiles as the granules of the presently claimed invention. In fact, the granules of *Villa* are an intermediate byproduct of the *Villa* invention and are not suitable for administration. For example, *Villa's* Example 1 recites granules consisting of mesalazine, carnauba wax and stearic acid (Page 7, lines 5-8). In the subsequent step, these granules are mixed with Carbopol and hydroxypropyl methylcellulose (Page 7, lines 9-11). The resulting granulates are dispersed as powder before a final mixing step that includes microcrystalline cellulose and magnesium stearate. The final step of the *Villa* process is tableting, followed by film coating the tablets with cellulose acetophthalate and a plasticizer (Page 7, lines 12-21).

The oral pharmaceutical formulation of the presently claimed invention comprises a granulate, a coating, and a sachet, wherein the coated granulate is packed in a sachet. Example 1 of the present application provides a preferred embodiment. In Example 1 the particulate granulate of the presently claimed invention comprises mesalazine, povidone, and ethylcellulose wherein the coating of ethylcellulose determines the release profile.

Villa does not meet each and every limitation of the presently claimed invention because it fails to disclose the administration of an oral pharmaceutical formulation in the form of a granulate, a coating, and a sachet, wherein the granulate comprises a pharmaceutically acceptable binder and more than 80% by weight of mesalazine or a pharmaceutically acceptable salt thereof, and the amount of coating is adjusted to the specific surface area of the granulate to achieve the in vitro release characteristics.

35 U.S.C. § 103(a)

Claims 4-5, 9-10 and 26 were rejected under 35 U.S.C. § 103(a) over Villa et al., WO 00/76481. In light of the arguments made above and for further reasons stated below, Applicants respectfully traverse this rejection.

Without acquiescing to the rejections and solely to expedite the prosecution, Applicants have amended claims 9 and 26 and canceled claim 4-5.

The Official Action asserts claim 9 would be obvious over the film coating taught by *Villa*. Applicants respectfully disagree. The film coating of the present invention is applied based on the desired release profile. At working Example 1 the specification states "in order to be able to determine the right amount of ethylcellulose necessary to apply on the granules to get the desirable dissolution rate profile, the surface area of the granules is measured prior to the coating process." (Column 16, lines 20-23). The Example further explains "The prediction of the quantity of coating that is necessary to apply on the granules has been developed based on the fact that there is a correlation between the amount of coating per surface area and the dissolution rate of the granules." (Column 16, lines 24-28). Thus, the coating of the presently claimed invention depends from the granulate size and the desired release characteristics.

By contrast, *Villa* utilizes the composition of the claimed tablet to ultimately control the release profile (Page 6, lines 20-34), not the coating. A skilled person would not modify a tablet formulation to obtain a coated granulate for a sachet as claimed.

The Official Action asserts the formulation of claim 10 would be obvious in light of *Villa*. Applicants respectfully disagree. Claim 10 recites a granulate consisting of mesalazine, a pharmaceutically acceptable binder and a coating. *Villa* recites a tablet consisting of no less than seven ingredients (Examples 1-5). Further, the composition of *Villa's* tablet is important to the tablet's release profile, not the coating.

The Official Action asserts the formulation of claim 26 would be obvious in light of *Villa*. Applicants respectfully disagree. The release profiles of claim 26 would not have been obvious because the release characteristics of the granulate of the presently claimed invention are achieved differently than the release characteristics of *Villa's* tablet. The presently claimed invention determines release profiles based on granulate size and coating (Example 1). The release profile of *Villa* is determined by the homogenous mixture and composition of matrixes (Page 6, lines 20-34).

Applicants submit claims 9-10 and 26 of the presently claimed invention are not obvious in light of *Villa* because *Villa* discloses a tablet not a particulate granulate, with at least seven

ingredients not three, whose release profile is determined by the composition of the matrixes not the granulate size and coating.

Claims 6 and 27-28 were rejected under 35 U.S.C. § 103(a) over Villa et al., WO 00/76481 in view of Augsburger et al., USU 2002/0177579. In light of the arguments made above and for further reasons stated below, Applicants respectfully traverse this rejection.

Villa discloses a tablet, not a granulate, with release characteristics determined by the composition of the matrixes, not coating. *Augsburger* discloses a process for producing a modified drug that is coated to different thicknesses or weights to produce subbatches. The subbatches are blended to achieve a specific drug release profile (Abstract). *Villa* and *Augsburger* are non compatible. A combination of *Villa* and *Augsburger* would result in a tablet of *Villa* that was coated to different thickness and weights of *Augsburger*. The resulting tablet would never achieve the desired release profile because the *Villa* tablet depends on the composition of the matrixes to achieve a release profile, not the blending of different coatings and weights.

By contrast, the presently claimed invention correlates the amount of coating to the desired release profile and surface area of the granulate. The release profile is not dependant on the composition of the matrixes nor the blending of tablets with different thickness and weights.

Applicants submit claims 6 and 27-28 of the presently claimed invention are not obvious over *Villa* in view of *Augsburger* because *Augsburger* does not overcome the deficiencies between the formulation of *Villa* and the presently claimed invention.

Claims 11 and 21 were rejected under 35 U.S.C. § 103(a) over Villa et al., WO 00/76481 in view of Valducci, US 2002/0034541. In light of the arguments made above and for further reasons stated below, Applicants respectfully traverse this rejection.

Applicants submit claims 11 and 21 are not obvious over *Villa* in view of *Valducci* because the tablets of *Villa* were never contemplated nor designed for packaging in a sachet.

Villa never contemplates the use of sachet because the *Villa* invention is directed to tablets, not granulates. The combination of *Villa* and *Valducci* would result in a tablet wrapped in a sachet.

The presently claimed invention discloses an oral pharmaceutical formulation in the form of a granulate that may be wrapped in a sachet. Applicants submit claims 11 and 21 of the presently claimed invention are not obvious over *Villa* in view of *Valducci* because a tablet of *Villa* wrapped in a sachet of *Valducci* is not an oral pharmaceutical formulation in the form of a particulate granulate as presented in the presently claimed invention.

Claim 29 was rejected under 35 U.S.C. § 103(a) over Villa et al., WO 00/76481 in view of Itoh et al., US 5,194,464. In light of the arguments made above and for further reasons stated below, Applicants respectfully traverse this rejection.

The presently claimed invention is inventive over the combination of *Villa* in view of *Itoh* because using povidone as a binder in the tablet of *Villa* would not arrive at the presently claimed granulates. If povidone was used in the formulation of *Villa*, the resulting formulation would still be a tablet, not a granulate, and the *Villa* tablet would still depend on composition of the matrixes for a release profile, not the granulate size and coating.

Applicants submit claim 29 of the presently claimed invention is not obvious over *Villa* in view of *Itoh* because *Itoh* does not overcome the deficiencies between the formulation of *Villa* and the presently claimed invention.

Claims 29-30 were rejected under 35 U.S.C. § 103(a) over Villa et al., WO 00/76481 in view of Jurgens, Jr. et al., US 5,316,772. In light of the arguments made above and for further reasons stated below, Applicants respectfully traverse this rejection.

The presently claimed invention is inventive over the combination of *Villa* in view of *Jurgens* because using a binder of povidone or a coating of ethylcellulose in the tablet of *Villa* would not arrive at the presently claimed granulates. If povidone was used in the formulation of *Villa*, the resulting formulation would still be a tablet, not a granulate, and the *Villa* tablet would

still depend on composition of the matrixes for a release profile, not the granulate size and coating.

Applicants submit claims 29 and 30 of the presently claimed invention are not obvious over *Villa* in view of *Jurgens* because the differences between the formulation of *Villa* and the presently claimed invention are not overcome by *Jurgens*.

Summary

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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Date

Mark DiPietro
Reg. No. 28,707
Merchant & Gould P.C.
P. O. Box 2903
Minneapolis, MN 55402-0903
(612) 332-5300

MD:RJF:kf

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